DERLEME REVIEW

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# Nutritional Burden in Tuberculosis and Inter-sectoral Nutritional Management for Tuberculosis Patients in Malaysia

Malezya'da Tüberkülozda Beslenme Yükü ve Sektörler Arası Beslenme Yönetimi: Malezya'da Bir Gözden Geçirme

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ABSTRACT Undernutrition and tuberculosis (TB) are a vital issue in most developing countries of the world. Both of these medical problems tend to have interacted with each other and bidirectional. The undernutrition creates a more significant problem in patients with active TB rather than among healthy individuals. Despite that, there is no protocol available on nutritional support in Malaysia to tackle on this issue. The objective of this review is to explore the nutrition burden of TB disease and the management available in Malaysia. The treatment for TB lasts for six months and above. Hence, it causes a financial burden not only for the healthcare provider but for the patient and the family members. If treatment is not successful and extends to a few months, it will increase the cost of the treatment. Malnutrition in TB patients will cause a problem in the outcome of TB treatment. It includes worsening of the disease, delayed sputum conversion, and increased risk of mortality. Other problems include malabsorption of Rifampicin, drug-induced hepatotoxicity, increased rate of relapse, and persistent of positive cultures in MDR-TB. Benefits of nutritional support for tuberculosis patients include improved body weight, increase in adherence/compliance to the tuberculosis treatment and increase in the success of the treatment. Implementation of nutritional support protocol by the government and Non-profit organization (NGO) will be beneficial and improve the quality of life of tuberculosis patients.

Malaysia

ÖZET Beslenme yetersizliği ve tüberküloz (TB) dünyanın gelişmekte olan birçok ülkesinde hayati bir konudur. Bu tıbbi sorunların her ikisi de birbirleriyle etkileşime girme ve çift yönlü olma eğilimindedir. Beslenme yetersizliği, sağlıklı bireylerden ziyade aktif TB'li hastalarda daha önemli bir problem yaratır. Buna rağmen, Malezya'da bu konuda mücadele edecek beslenme desteği konusunda protokol bulunmamaktadır. Bu derlemenin amacı TB hastalığının beslenme yükünü ve Malezya'da bulunan yönetimi araştırmaktır. TB tedavisi altı ay ve daha uzun sürer. Dolayısıyla, sadece sağlık hizmeti sağlayıcısı için değil, hasta ve aile üyeleri için finansal bir yüke neden olmaktadır. Eğer tedavi başarılı olmaz ve birkaç aya kadar uzarsa, tedavinin maliyetini yükseltir. TB hastalarındaki yetersiz beslenme, TB tedavisinin sonucunda bir soruna neden olacaktır. Hastalığın kötüleşmesini, balgam dönüşümünü geciktirmeyi ve ölüm riskini arttırmayı içerir. Diğer problemler arasında Rifampisin salgılanması, ilaca bağlı hepatotoksisite, artmış nüks oranı ve MDR-TB'de pozitif kültürlerin kalıcılığı bulunur. Tüberküloz hastaları için beslenme desteğinin faydaları arasında vücut ağırlığının iyilestirilmesi, tüberküloz tedavisine uyumun artması ve tedavinin başarısının artması yer alır. Devlet ve sivil toplum kuruluşları (STK) tarafından beslenme destek protokolünün uygulanması yararlı olacak ve tüberküloz hastalarının yaşam kalitesini artıracaktır.

Keywords: Malnutrition; nutritional status; tuberculosis; Anahtar Kelimeler: Kötü beslenme; beslenme durumu; tüberküloz; Malezva

ndernutrition and tuberculosis (TB) are a major issue in most developing countries of the world. Both of these medical problems tend to interact with each other and bidirectional. The undernutrition problem is more significant in patients

with active TB compared to non-TB persons.1 Undernutrition can cause secondary immunodeficiency that increasing the risk of getting infection.<sup>2</sup> Patient with active TB and malnutrition was associated with reduced appetite, reducing the absorption of nutrients,

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and affects metabolism that can lead to waste.<sup>3</sup> Both macro- and micronutrient deficiency especially protein-energy malnutrition enhance the risk of complications in TB patients.<sup>4</sup> It was found that the undernourished TB patients demonstrate slow recovery process and increased mortality rate as compared to the normal TB patients.<sup>5</sup> Hence, by giving a supplementation of nutrition can enhance rapid recovery in TB patients.<sup>6,7</sup>

Malnutrition defines a nutritional state in which energy, protein, and other nutrients' (macro and, micro-nutrient) imbalance, either deficiency or excess causes negative effects on our body or tissues (size, composition, and shape), physiological function and medical outcome.<sup>8</sup> Generally, undernutrition appears to be low weight-for-height, and this condition often coexists with micronutrient deficiency, which is commonly known as clinical malnutrition or protein-energy malnutrition.<sup>9</sup> General undernutrition can affect significantly the immunity process such as cell-mediated immunity, counts of antibodies, phagocyte function, and production of cytokine.<sup>8</sup>

TB has a dramatic effect on the nutritional status in the majority of studies investigating the association between TB and body composition in patients affected. It was found in a research that undernourished patients with TB tend to have delayed recovery process and increased mortality in comparison with well-nourished patients.<sup>10</sup> Undernutrition and TB have a two-way relationship. Undernourished is one of the significant risks for the conversion of active TB from the latent TB infection. TB can cause weight loss and loss of nutrition.<sup>11</sup> This malnutrition contributes undoubtedly to mortality and morbidity, especially in poor resource environment. The effect of primary undernutrition on TB can raise the occurrence risk to both of population and clinical manifestations of TB disease.

The connection between TB and undernutrition has established. Malnutrition weakens immunity that folds the risk of progression of latent TB to active TB.<sup>4</sup> Before the onset of the TB disease, the nutritional status of the patient is hard to measure accurately. Making it difficult to determine whether undernutrition has caused the development of the TB or vice versa.<sup>12</sup> Loss of weight is one of the significant symptoms of TB. In a study in Los Angeles county, nearly half suffered weight loss and also had anorexia. TB also associated with reduced body mass index (BMI) due to loss of combining both of fat-free mass and fat mass. The occurrences of moderate to severe undernutrition in the first four weeks of treatment regime of active TB has been found to be a significantly associated factor for mortality.<sup>11</sup>

Poverty has long linked to undernutrition and TB.<sup>13,14</sup> Access difficulty to healthcare services, food insecurity, and poverty lead to TB disease. There is a bidirectional connection between TB and poverty; the poor are more likely to suffer from TB, and those with TB are more likely to become poor.<sup>14</sup> Studies recommend that the average TB patients loss about three to four months of household financial gain because of incapability due to the TB disease and to cover the cost for the TB treatment.<sup>15,16</sup> TB patients that are living at lower poverty level (<US\$ 1.25 per day) might face a dilemma of using their income between buying foods or treating themselves with anti-TB for at least six months. Unfortunately, in addition to being a risk issue for the event of TB disease, poverty may adversely affect the treatment outcomes.<sup>17</sup>

## ECONOMIC BURDEN IN TUBERCULOSIS MANAGEMENT

The duration of TB treatment lasts for six months and above. It involves a higher cost for the healthcare provider and also to the patient and caregiver. If treatment is not successful and extends to a few months, it will increase the cost of the treatment.

Patient cost for pre-diagnostic TB varied widely depending on the country, which is from USD\$ 36 in Malawi to USD\$ 109 in Zambia and USD\$ 196 in Ethiopia. This average cost for pre-diagnosis of TB disease was 11.3%, 10.6%, and 35.0% respectively of the average annual income of the patient. Interestingly, when the average cost of pre-diagnosis of TB in Malawi was compared between the poor and the non-poor, poor tuberculosis patients spent one-fifth of their average annual income, which is 9% higher than the average of TB patient spending.<sup>18</sup> The average post-diagnostic cost of patients in Ethiopia in South Africa was between USD\$ 17 and USD\$ 488. Five trials were done estimating the cost of pre-/post-diagnosis TB care for patients. The total cost of treatment for patients was between USD\$ 3 and USD\$ 662, the majority of which was less than USD\$ 100. The overall average cost of post-diagnostic compared to the annual income of patients reported in between 2.8 per cent in Zambia and 30.0 per cent in Sierra Leone.<sup>18</sup>

Studies conducted in Penang, Malaysia in 2008 found that the average total cost of treatment for pre and post-diagnostic per TB patient was USD\$ 916.40. The cost of anti-TB medication accounts for the highest cost of public health services. The cost of transport to the TB clinic was the major part of the price that absorbs by the patient. This study also showed that the expenses by TB patients accounted for about 80 per cent of the total cost of TB care compared to 20 per cent cover by public health services.<sup>19</sup>

About 75-80% of cases of TB occurred in the working-age group, particularly in the underdeveloped region. The impact of TB on patient's economic from direct and indirect costs majority due to income loss due to inability to work (average loss around 20-30 per cent of household income annually) and premature deaths (15 years of lost revenue). Studies from a developing country have demonstrated that the average cost of treating TB ranges from USD\$ 276 to USD\$ 1,546 and higher cost for multidrug-resistant TB (MDR-TB) with USD\$ 1 thousand to USD\$ 10 thousand.<sup>19</sup>

## NUTRITIONAL STATUS AND TUBERCULOSIS

Catabolic processes that cause wasting usually begin during active tuberculosis before the patient is diagnosed; therefore, the patient's nutritional status at the time of diagnosis is more known than the wasting process itself.<sup>20</sup> Like human immune-deficiency virus (HIV), the metabolic rate or energy expenditure at the time of diagnosis is high, resulting in more calorie requirements to archive minimal body requirements for normal function. During that time, nutritional or energy consumption or food intake is likely to decrease because of disease-related anorexia.<sup>21</sup> The mixture of events will lead to loss of weight and, if the energy consumption becomes static or energy consumption is reduced, it will lead to a waste. Luckily, pro-inflammatory cytokines counteract this negative process, the use of amino acids and protein synthesis will be inhibited.

The Ministry of Health Malaysia has classified body mass index (BMI)-based nutritional status as shown in Table 1.<sup>22</sup> There is a study that shows the patients with TB, had significantly lower BMI compared to controls. The lean body mass in TB patients was significantly lower than in controls. The loss of fat in TB patients is shown by a significant reduction in the mid-upper arm circumference (MUAC), the thickness of the skin and the fat mass index. Patients with tuberculosis have a significantly lower creatinine and serum albumin index compared to controls. It concludes that TB patients have reduced body weight significantly with loss of lean body weight, fat weight and low creatinine and serum albumin index.<sup>23</sup>

Several studies have found that active TB patients have less BMI compared to well-nourished people.<sup>24</sup> In a study from Indonesia, the average BMI of the patients with active TB was one fifth lower than in controls. A total of one-third of TB patients had<18.5 kg/m<sup>2</sup> of BMI, which is 6-fold higher compared to the controls. Also, in those with active TB, weight, skinfold thickness, MUAC, fat-free mass and fat mass were all low compared to the controls.<sup>1</sup> One study done in Ethiopian with sample of 155 of active TB patients (74 TB / HIV co-infected and 81 HIV-negative) and 31 controls, found the underweight patients was high (65.4% of TB, 71.6% of TB /HIV

<b>TABLE 1:</b> Classification of weight by BMI (Malaysia).	
Classification	BMI (kg/m²)
Underweight	<18.5
Normal	18.5-22.9
Overweight	≥23
Pre-obese	23.0-27.4
Obese I	27.5-34.9
Obese II	35.0-39.9
Obese III	≥40

BMI: Body mass index.

co-infected) and extreme underweight (BMI<16 kg/m<sup>2</sup>) also more significant in co-infected patients.<sup>25</sup> R Visvanathan et al. reported that about 14 percent of seniors had BMI <  $18.5 \text{ kg/m}^{2.26}$ 

In Malaysia, few studies were conducted to evaluate BMI in the healthy population. There was a lack of Malaysian's studies comparing the BMI of TB patients and the healthy population. In the earlier study, 60-64 per cent of the Malaysian adult population had healthy BMI, 11-20 per cent were underweight, and 29-30 per cent were obese.<sup>27</sup>

## PREVALENCE OF MALNUTRITION IN TUBERCULOSIS PATIENTS

TB is linked to various socioeconomic factors, such as poverty, poor housing, and economic deprivation, resulting in poor nutritional status and impaired immune function. Nutrition is essential for the wellbeing and physiological function of all body systems including the immunity.<sup>28</sup>

A cross-sectional study in Ethiopia stated that undernutrition prevalence for TB patients was 39.7% namely 23.6% with mild undernutrition, 8.6% moderate undernutrition, and 7.2% severe undernutrition. From this study also, we can conclude that the prevalence of underweight and obesity is varying among the elderly, adults and teenagers' groups. The evidence of a strong relationship between BMI and morbidity suggests that BMI can be used as part of the evaluation of the nutritional burden in TB patients.<sup>28</sup>

This study showed that approximately one-fifth of TB patients did not meet the requirement of the calories according to Recommended Dietary Allowance (RDA). In the early treatment, approximately one-third of the patients were underweighted. Subsequently, after treatment, it reduced to 21.8% only. The median BMI was 20.99 kg/m<sup>2</sup> (SD±5.81).<sup>29</sup>

A large rural cohort in central India evaluated the nutritional status among adult TB patients by using dietary intake, nutritional status, and weight gain data.<sup>9</sup> The study reported that the median weight and the median BMI in men was 42 kg and 16.0 kg/m<sup>2</sup>, respectively. Meanwhile, the median weight and the median BMI in women was 34.1 kg and 15.0 kg/m<sup>2</sup>, respectively. One-half of the patients with MDR-TB

had an underweight BMI. Given these cases of TB in India are higher in the poor group who are also higher in food insecurity. These low BMI at diagnosis and minimal weight increase, majority patients with active TB in India do not attain normal nutrition status and are prone to be underweight even after the treatment is completed.<sup>30</sup>

In Malaysia, there are a few studies that showed that the average BMI for TB patients was lower than the average of healthy population. Characteristics of TB patients in Penang General Hospital, Malaysia are as follows; the weight in kg [mean standard deviation (SD)] was 50.96±12.40 only and age in years (mean SD) was 44.97±17.13.<sup>31</sup> A study in Kota Kinabalu, Sabah, Malaysia carried out among 176 consenting participants in Kota Kinabalu Health Clinic found that the mean BMI (kg/m<sup>2</sup>) (BMI range) was 18.1 kg/m<sup>2</sup> (10.0-31.1) which is underweight. Mean BMI for the average population in Malaysia in 2009 was higher than that of TB patients. The overall mean body weight and BMI for adult Malaysians aged 18-59 years old were 62.65 kg and 24.37 kg/m<sup>2</sup> respectively.<sup>32</sup>

## UNDERNUTRITION AND TUBERCULOSIS OUTCOME

Nutritional status convalescence and gaining weight arise during TB therapy. However, it remains uncertain whether weight gains can be used as a therapy marker. No microbiological reaction or relapse was observed during treatment to influence weight gains. Studies have found that weight change over time is a predictor of the outcome of the treatment significantly even after the confounder has adjusted. The less than 5 per cent increase in weight in underweight patients during the intensive phase of TB treatment was also contributing to the increased risk of relapse.<sup>33</sup>

The effect of TB treatment on weight can be influenced by insufficient nutrients intake. For example, a study done in Tanzania, TB patients experienced weight gain during TB treatment, but these increase in weight persisted if patients were hospitalised. It is probably due to better intake of nutrient during admission.<sup>11</sup>

Although the pathophysiology is still not clear, these patients need nutrition support during the 6

months of therapy in addition to the anti-TB regime. These may include clinical measures to achieve nutrition improvement. Besides, nutrient intake may have more to do with a fair distribution of resources and the involvement of the community in healthcare, especially in poor resource environments. Increased understanding of how patients gain weight during TB treatment can give a clear picture of the relationship between TB and malnutrition.<sup>11</sup>

#### UNDERNUTRITION AND IMMUNE FUNCTION

Nutrition status is one of the essential factors that contribute to the treatment outcome. Nutrient deficiency is well known to link to impaired immune function. Malnutrition will weaken immune function by reducing cell-mediated immunity and thus increase infection susceptibility. However, malnutrition also can contribute by recurrent infections, chronic inflammation, and disordered nutrient assimilation disorder.<sup>34</sup>

#### UNDERNUTRITION AND ADVERSE DRUG REACTIONS

The most effective anti-TB therapy is a combination of anti-TB drugs (Isoniazid, Rifampicin, and Pyrazinamide) that is given for eight weeks during the intensive phase followed by 4-7 months of maintenance phase of anti-TB drugs (Rifampicin and Isoniazid).<sup>35</sup> Despite the development of this good regime, TB treatment remains a problem in patients that do not tolerate medication.<sup>36</sup> This problem linked to significant adverse drug reactions (ADRs).<sup>36</sup> An ADR is any adverse drug effect beyond its expected therapeutic effects during clinical use.<sup>37</sup> Common ADRs for TB medications reported in previous studies are nausea/vomiting, skin rash and pruritus, arthralgia and neuropsychiatric symptoms, hepatitis and thrombocytopenia.<sup>38</sup>

Predicting the risk factors for ADR to first-line TB therapy can help to identify patients who need proper monitoring to prevent possible morbidity, hospitalisation, and death. Previous studies have shown that female, age more than 60 years, Asian birth, low BMI and HIV infection are the associated risk factors that contribute to the occurrence of ADRs in anti-TB drugs.<sup>39</sup> Malnutrition will lead to a reduction in drug clearance, which increases the concentration of the anti-TB drugs in the plasma level and the risk of ADRs later.<sup>40</sup>

#### UNDERNUTRITION AND HEPATOTOXICITY

A few kinds of research in India discovered that malnutrition is an associated factor in the progression of drug-induced hepatotoxicity, which is one of the side effects of anti-TB treatment. In a recent research, the risk of drug-induced hepatotoxicity in patients with BMI below 17 kg/m<sup>2</sup> was five times greater. Druginduced hepatotoxicity can interrupt the TB treatment and increase the risk for defaulter. Nutritional status may also affect the drug pharmacokinetics of anti-TB medication. In undernourished patients in India, lower concentrations of some drugs such as Rifampicin have been recorded.<sup>41</sup>

#### UNDERNUTRITION AND DELAYED SPUTUM CONVERSION

A systematic review done in 2018 found that another risk factor for delayed sputum conversion is low BMI. Low BMI is significant in people with malnutrition and possibly leads to lower immunity.<sup>42</sup>

### UNDERNUTRITION AND MULTI-DRUG RESISTANCE (MDR)

A study shows that patients' nutritional status is a significant predictor of treatment effectiveness in drugresistant TB. The BMI below 18.5 kg/m<sup>2</sup> as a marker for poor nutritional status in patients with TB at the early therapy was described in numerous studies as a risk factor for poor results of treatment.<sup>43</sup>

#### UNDERNUTRITION AND RELAPSE

There is a study found that the risk of relapse was high among those diagnosed with underweight (19.1 vs. 4.8 per cent) or with a BMI of less than 18.5 kg/m<sup>2</sup> (19.5 vs. 5.8 per cent). The increase in weight between diagnosis and completion of 2-month intensive phase TB therapy was associated with an increased risk of relapse (18.4 vs. 10.3 per cent). In conclusion, increase in weight of less than 5 per cent during the first two months of treatment was associated with an increased risk of relapse among people who were underweight at diagnosis. This risk factors were easily identified, even in poor resource environment.<sup>44</sup>

#### UNDERNUTRITION AND MORTALITY

A study done in Malawi found that wasting in active TB patients is linked to increased mortality. In newly diagnosed 1.181 TB patients, 57 per cent were underweight in rural Malawi (BMI<18.5 kg/m<sup>2</sup>), in which 21 per cent were having BMI<16.0 kg/m<sup>2</sup>. A BMI of less than 17.0 kg/m<sup>2</sup> or moderate to severe undernutrition double the risk of early death.<sup>5</sup> In another research from Malawi, advanced lung findings were related to low BMI and fat mass.<sup>45</sup>

Several studies have shown that malnutrition indices are the associated factors for mortality in TB patients. Moderate to severe malnutrition was found as the associated factors for mortality in the first month of the intensive phase of TB treatment.<sup>5</sup> In Mexico, a weight loss of more than 15% and in India, a weight of less than 35 kg at diagnosis was associated with increased TB fatality. While in Zambia, a weight of more than 55 kilograms was a positive predictive factor of a good outcome. In Brazil, the study showed that serum albumin levels predict inhospital mortality in TB patients upon admission. A similar association was also seen in France and Taiwan. A study in Guinea Bissau showed a gradual increase in the risk of death by using both the MUAC and the BMI measurement.<sup>46</sup>

In rural and central India, moderate to severe undernutrition increases the risk of TB-related deaths. The results were consistent in children and adults, patients with and without HIV infection, and patients with both drug-sensitive and drug-resistant TB. A weight of less than 35 kg was associated with an almost four-fold death risk in South India compared to weight more than 35 kg. In conclusion, the risk of death was double that in severely undernourished patients who received anti-TB therapy.<sup>46</sup>

Table 2 summarises the effect of undernutrition on outcomes in tuberculosis.

## BENEFIT OF NUTRITIONAL SUPPORT DURING TUBERCULOSIS TREATMENT

The cost of treatment for TB correlates with the increase in the duration of therapy (the longer the length, the higher the cost of treatment). Nutritional support will help to reduce the cost indirectly by improving nutritional status.

<b>TABLE 2:</b> Effect of undernutrition on outcomes in tuberculosis.	
Effects on disease:	
Increased severity of the disease	
Increased risk of death	
Effects of treatment:	
Delayed sputum conversion	
Risk factor for drug-induced hepatotoxicity	
Malabsorption of rifampicin	
Reversion of positive cultures in MDR-TB	
Effects on long-term outcomes:	
Increased rate of relapse	
Effects on contacts:	
Increased incidence in undernourished contacts	

#### NUTRITIONAL STATUS AND IMPROVED BODY WEIGHT

Nutrition supplementation may improve the bodyweight of TB patients. A study found that nutrition counselling to raise the energy usage and combine with supplementation resulted in a significant weight gain, increase in the total lean mass and physical function after six weeks during the initial phase of TB treatment. Subsequently, patients in the nutrition supplementation group continued to show weight gain more compared to control during follow-up.<sup>47</sup>

Another study found that the patients in the nutrition support group (n=19) increased their weight significantly. At week 6, grip strength and total lean mass also considerably increased compared to the controls. The weight gain in the nutrition support group was higher during the follow-up, but this improvement was primarily due to an increase in fat mass in the dietary supplement group compared to the control group.<sup>24</sup>

In the therapy of TB, vitamins and minerals may play a significant role. One research showed that vitamin C and E support had enhanced the immune response to TB in combination with TB treatment.<sup>4</sup> These studies also found that vitamin A and zinc supplementation improved the efficacy of anti-TB drugs in the first two months.<sup>4</sup>

Nutritional supplementation can be a new approach to the quick recovery of TB patients. In conclusion, by increasing the population's nutritional status, TB control, especially in underdeveloped regions of the world, could prove to be a useful measure.

# NUTRITIONAL STATUS AND ADHERENCE/COMPLIANCE OF TREATMENT

It was shown that both financial and non-financial incentives enhance compliance among poor communities in the United States (USA) with the supervised treatment system known as directly observed shortcourse therapy (DOTS).<sup>48</sup> Another research in the United States showed that the rising number of treatment benefits led to a reduction in the default treatment rate.<sup>49</sup> The non-compliance rate was significantly lower in the incentive group compared to controls (13 vs. 30 per cent). The findings showed that food basket allocation could be a beneficial approach to improve adherence to TB treatments in primary care.<sup>50</sup>

#### NUTRITIONAL SUPPORT AND CURE RATE

A retrospective comparative study was carried out among 142 patients at the Duque de Caxias primary hospital in Brazil. There were 2 groups of samples: The first group consisted of 68 patients with conventional regimens, and the second group consisted of 74 patients receiving the same regimens but receiving monthly food baskets. The analysis between the two groups found that the cure rate was higher compared to standard regime group (87.1% vs. 69.7%) in food basket group.<sup>50</sup>

## TRIAL OF NUTRITIONAL SUPPORT PROGRAMME

#### WORLDWIDE

In Brazil, a trial study was conducted by dividing the samples into two groups. The first group consisted of 68 subjects who only received the recommended standard of treatment. Another group consisted of 74 subjects, comprising those receiving the same treatment regimen administered in the first group plus non-perishable food baskets. A unit cost of R\$30.00 in Brazilian reals (R\$) was distributed monthly to the food baskets.<sup>50</sup>

There was a study in two Indian TB units by a non-profit organization (NGO) supplied TB patients with monthly rice (13 kg) and lentil beans (3 kg) for

60 to 90 days at no price. Of the 173 patients receiving dietary incentive for TB, only 15 (9%) had negative results. Compared to the non-nutritional support group, 84 (21%) had unsuccessful therapy results which is low statistically significantly. After adjustment for age, sex and prior treatment, those receiving nutritional support were nearly 50% less likely to receive unsuccessful treatment than those receiving no nutritional support (RR: 0.51; 95% CI: 0.30-0.86). This research discovered that nutritional support for poor patients was associated with a lower risk of TB treatment failure. The basic supply of \$10 per month of rice and lentil beans was combined with a significantly reduced risk of unfavourable treatment outcomes, even after adjustment for other associated factors.17

#### NUTRITIONAL SUPPORT IN MALAYSIA

#### a) Government

There was no nutritional support trial or intervention for TB patients in Malaysia. The management or referral of undernourished TB patients was also not included in the Malaysian Clinical Practice Guidelines for TB. However, there is a similar nutritional support program for malnourished children. The programmed is called "The Program for the Rehabilitation of Malnourished Children (PPKZM)." It was introduced in 1989 by the Malaysian government as an attempt to enhance the health and nutritional status of kids aged six months to less than six years of hard-core low-income households. This program provides food support to children who meet the eligibility criteria to obtain healthy and nutritious food to achieve optimum physical and mental growth. Children will also receive treatment (if they suffer from illness), immunisation, health education, and health care, as well as rigorous supervision. Every child deserves to be supplied with food baskets such as rice, breakfast cereals, biscuits, margarine, eggs, multivitamins, sardines, anchovies, rice noodles, chocolate malt powder, cooking oil, fresh fruits, and vegetables or milk. Other organisations such as Pusat Pungutan Zakat (PPZ) or Malaysian Zakat Collection Centre also can contribute to cover the cost of nutritional support such as food basket. They have budget or allocation for medical welfare program such as Medical Treatment Assistance. They can use this budget for patients because nutritional support is one of the managements for TB, especially for the lower economic status, but not covered by Ministry of Health.

#### b) Non-Governmental Organization (NGO)

Sabah Anti Tuberculosis Association (SABATA) is one of the Malaysian NGOs that help TB patients. They will support patients, especially in the form of financing for the patients' transportation to get treatment at the nearest TB clinic. The primary function of this NGO is to provide a welfare service that helps people who suffer from TB and to raise funds to finance TB treatment in Sabah. They can broaden their financial support activity to improve the nutritional status of TB patients. A study in Kota Kinabalu showed that travel expenses, time spent travelling to treatment centres and family members who had the disease affect compliance with DOTS.<sup>51</sup> The nutritional support program will increase compliance and adherence to tuberculosis treatment.

## NUTRITIONAL SUPPORT PROTOCOL

#### WHO RECOMMENDATIONS

#### a) Nutritional Assessment and Counselling

During diagnosis and therapy, the World Health Organization (WHO) suggested that all individuals with active TB receive their dietary status assessment and proper management based on their dietary status. Nutritional evaluation is an essential dietary care requirement. There is no evidence that the dietary management of severe acute malnutrition in active TB patients should distinguish from the non-TB malnutrition patient.<sup>30</sup>

#### B) Management of Severe Acute Malnutrition

WHO suggests treating severe acute malnutrition for school kids and teenagers (age 5-19) and adults with active TB and severe acute malnutrition, including pregnant and nursing women. Children under five years of age with active TB and severe acute malnutrition should also be managed to follow the suggestion of the WHO for the management of severe acute malnutrition in children under five years of age.<sup>30</sup>

#### C) Management of Moderate Undernutrition

Adherence and comorbidity should be evaluated for school kids, adolescents and adults with active TB and mild undernutrition who have not recovered standard BMI after two months of therapy, including lactating females, and those who lose weight during treatment. If indicated, they should also be evaluated and recommended the nutritional supplied with extra nutrient-rich or fortified foods to restore normal nutritional status. Children under the age of five should handle same as other undernourished kid with active TB and mild undernutrition. These include local food supplements available that are rich in nutrients or fortified to restore the correct height. For the restoration of ordinary dietary status, nutrient-rich or fortified additional foods should be given locally in patients with active MDR-TB and mild undernutrition. Pregnant women with active TB and mild malnutrition or with insufficient weight gain should be supplied with locally available supplementary fortified foods or nutrient-rich to achieve an average weekly minimum weight gain of about 300 g.30

#### D) Micronutrient Supplementation

Multiple nutrient supplements should be given in circumstances where fortified foods must be supplied but not accessible following WHO standard management of mild undernutrition. According to the WHO, all pregnant females with active TB should receive multiple folic acids and iron supplements and other mineral and vitamins to satisfy their mother's micronutrient requirements.<sup>30</sup>

#### E) TB Contact Investigation

In situations where contact tracing is carried out, nutrition screening and evaluation should be carried out in the context of TB contact research by household contacts of people with active TB. If malnutrition is detected, it should be managed according to WHO guidelines.<sup>30</sup>

Summary regarding the nutritional support protocol adopted from WHO guidelines is stated in Table 3.

#### DISCUSSION AND RECOMMENDATIONS

Recommendations for governmental organisations

We need to have linked programs between the Ministry of Women & Child Development and the

TABLE 3: Summary of nutritional management protocol.	
Summary regarding the nutritional support protocol adopted from WHO guidelines stated in Box 2.	
i) Nutritional assessment	
<ul> <li>Clinical assessment of nutritional status-nutrition-oriented history and examination</li> </ul>	
<ul> <li>Anthropometric measurements in children and the classification of nutritional status using WHO-recommended cut-offs.</li> </ul>	
• Anthropometric measurements in adults and classification of nutritional status according to ranges of BMI appropriate for Malaysian populations.	
• Use of mid-upper arm circumference for classification of nutritional status in patients who are unable to stand or in whom BMI is inappropriate (preg-	
nant women, patients with oedema).	
<ul> <li>Clinical and nutritional indicators that need for hospitalisation care (red flags).</li> </ul>	
ii) Nutritional counselling	
• Proper nutritional counselling should be provided to tuberculosis patients along with nutritional support for severely malnourished patients and regula	
nutritional assessments of tuberculosis patients.	
<ul> <li>Concept of a healthy balanced diet.</li> </ul>	
• Understanding the impact of tuberculosis on nutritional status and importance of nutritional recovery in patients with tuberculosis.	
<ul> <li>Advice on increasing energy consumption through diet by using locally available nutrient-rich food.</li> </ul>	
· Understanding foods and practices to avoid and clarify myths and misconceptions including expenses on costly fruits, costly tonics, commercial food	
supplements and IV fluid therapy.	
• Understanding the role of physical activity in strengthening muscles and improving appetite.	
iii) Nutritional management in general	
<ul> <li>Recommended energy, protein and micronutrient intake in patients with active tuberculosis.</li> </ul>	
<ul> <li>Management of moderate to severe undernutrition in patients with a food basket.</li> </ul>	
• Management of severe undernutrition requiring hospitalisation-initial stabilisation phase and rehabilitation phase.	

Ministry of Health and Family Welfare to identify joint beneficiaries. For example, the 1 Azam Food Basket program can be expanded to undernourished TB patients and not limited to malnourished children under five years. Recently, there was a reduction in the number of receivers of food basket among undernourished children. Therefore, the budget can be diverted and allocated to malnourished TB patients. The proposed household food baskets for malnourished TB patients must:

a) Meet 50 per cent of the RDA for cereals, pulses, and edible oil, taking into consideration local preferences. Different types of legumes and oils can issue on a rotation basis.

b) Fortify the staple food mainly rice or wheat in the food basket especially for TB/HIV patients with micronutrients and vitamins such as vitamin A, vitamin D, calcium and

c) Consider supplying locally preferred and homegrown food rather than supplying the same type of food items across the country. Therefore, with the supply of food basket for undernourished tuberculosis patients, we recommend government agencies/the Ministry of Health to:

(i) Support pilot implementation project (food basket) and generate evidence;

(ii) Do the cost-effectiveness analysis regarding nutritional support among the undernourished TB patients;

(iii) Collaborate with other ministries and agencies at the policy level;

(iv) Provide technical support and guidance (CPG) for the management of undernourished tuber-culosis patients.

(v) Develop apps for the nutritional management of undernourished TB patients. These will help in the assessment, counselling, and management of nutrition problems among TB patients. India country already has the apps that they call N-TB that simplify the nutritional care of adult patients with TB. We also recommend the extension of this food basket program not only for active TB but also for HIV control programs and contact or latent TB patients to ensure nutrition and food adequacy especially in the process of preventing active TB. The BMI of TB contact or latent TB patients should be monitored closely. Regular follow up, and intervention should be performed if there is an undernourished contact to prevent them from developing active TB.

There should be a broadening of the scope of nutritionist and dietician (dietitian referral) not only limited to chronic diseases but also to deal with the patients with infectious diseases who have nutritional deficiencies through hospitalisation, therapeutic feeding, and nutritional rehabilitation. The protocol for the management of undernutrition in tuberculosis patients should be developed and standardised. Mainstream nutrition and food security assessments should be embedded in Malaysian health programs. Priority must be given to beneficiary groups most vulnerable to nutritional challenges such as tuberculosis or HIVinfected patients for maximum and long-term impact of nutrition intervention.

#### **RECOMMENDATIONS FOR PRIVATE SECTOR/NGO**

a) Collaboration with the local community to empower volunteers/program need empowerment. It can help to mobilise domestic resources in the form of sponsors who can support at least one TB patient with one meal daily until completing their treatment.

b) Local NGOs like SABATA can help the government to supply food baskets for tuberculosis patients.

c) Development of low-cost highly nutritious products using indigenous food such as nutritious bars, chews, cookies, etc. and training of self-help groups to produce, promote, and market such products.

d) As a corporate social responsibility, companies can adopt all TB patients in a few villages or districts and provide them with nutritional support or vouchers for a meal.

e) Recommendations for academia, universities, and research agencies, etc. to generate evidence on the following areas: (i) Clinical trials to produce evidence on the effect of nutritional intervention on TB outcome;

(ii) Plan research activities to develop and use nutrient-rich products;

(iii) Collaboration with industries to create nutrition and food security assessment, screening and training tools such as a checklist to identify vulnerable populations;

(iv) Research regarding the magnitude of malnutrition problem in Malaysian TB patients and also the link between malnutrition and infectious diseases such as TB and HIV;

(iv) Take steps to convert the evidence to a policy by collaborating with a health policymaker.

Recommendations to family members/society

(i) rovide education and awareness to the public about the importance of nutrition in TB infection.

(ii) Community-based programs to empower their knowledge on the benefits of adequate food, healthy food, and nutritional intake, thereby avoiding both under-nutrition and over nutrition.

(iii) Involvement of DOT providers, both family, and community, in nutritional support and counselling programs for TB patients.

(iv) Organise outreach programs/ activities to increase accessibility, awareness of balanced food, and nutrients to the public.

(v) Capacity building through the organisation of community that helps the government in getting the fortified food for food basket in the targeted tuberculosis patients.

Critical gaps in existing programs/ Difficulty in implementation

(i) Government programs usually are vertical. Low cross-linkages exist, and no program supports patients with tuberculosis.

ii) The nutritional aspect is often not covered in the Infectious Diseases Health Programme. The plan is more inclined to NCD.

iii) There is a lack of interaction between civil society, corporate or private sectors, and government programs.

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vi) Lack of awareness on the importance of nutrition for the prevention and control of infectious diseases, both patients and healthcare providers.

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Undernutrition in TB can cause many problems. Most TB patients have a low income. TB disease will increase the patients' financial burden, and this causes them to cut the budget for food and expose them to malnutrition.

Not all patients need nutritional support, but those with healthy BMI usually need to be monitored closely. There is no evidence of a difference in dietary support for TB patients compared to healthy people. Concern about weight loss, should lead to further clinical assessment of the causes of undernutrition (e.g. comorbidity, TB drug resistance, low adherence,) and dietary evaluation to identify the most suitable intervention. If the nutrition indices approach the cut-off value for diagnosing severe acute malnutrition, should considered close monitoring nutrition status and nutrition support as early as possible (before completion of the first two months of TB treatment).

Nutritional evaluation is an essential requirement for dietary care provision. TB requires to be treated for at least six months. Patients need assistance not only for psychology but also for economics and nutrition. Policymakers and stakeholders need proof from fundamental and clinical sciences, epidemiological and operational concentrations that require extra nutritional supplements and support for active TB patients.

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No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

#### Authorship Contributions

Idea/Concept: Khalid Mokti, Zaleha Isa, Mohd Rizal Abdul Manaf; Control/Supervision: Zaleha Isa, Mohd Rizal Abdul Manaf; Literature Review: Khalid Mokti; Critical Review: Firdaus Hayati, Syed Sharizman Syed Abd Rahim.

- REFERENCES
- Karyadi E, Schultink W, Nelwan RH, Gross R, Amin Z, Dolmans WM, et al. Poor micronutrient status of active pulmonary tuberculosis patients in Indonesia. J Nutr. 2000;130(12): 2953-8. [Crossref] [PubMed]
- Chan J, Tanaka K, Mannion C, Carroll D, Tsang M, Xing Y, et al. Effects of protein calorie malnutrition on mice infected with BCG. Journal of Nutritional Immunology. 1997;5(1):11-9. [Crossref]
- Paton NI, Castello-Branco LR, Jennings G, Ortigao-de-Sampaio MB, Elia M, Costa S, et al. Impact of tuberculosis on the body composition of HIV-infected men in Brazil. J Acquir Immune Defic Syndr Hum Retrovirol. 1999;20(3):265-71. [Crossref] [PubMed]
- 4. Gupta KB, Gupta R, Atreja A, Verma M, Vishvkarma S. Tuberculosis and nutrition.

Lung India. 2009;26(1):9-16. [Crossref] [PubMed] [PMC]

- Zachariah R, Spielmann MP, Harries AD, Salaniponi FM. Moderate to severe malnutrition in patients with tuberculosis is a risk factor associated with early death. Trans R Soc Trop Med Hyg. 2002;96(3):291-4. [Crossref] [PubMed]
- Karyadi E, West CE, Schultink W, Nelwan RH, Gross R, Amin Z, et al. A double-blind, placebo-controlled study of vitamin A and zinc supplementation in persons with tuberculosis in Indonesia: effects on clinical response and nutritional status. Am J Clin Nutr. 2002;75(4):720-7. [Crossref] [PubMed]
- Safarian MD, Karagezian KG, Karapetian ET, Avanesian NA. [The efficacy of antioxidant therapy in patients with tuberculosis of the lungs and the correction of lipid peroxi-

dation processes]. Probl Tuberk. 1990;(5):40-4. [PubMed]

- Meier R, Stratton R. Basic concepts in nutrition: epidemiology of malnutrition. Clin Nutr ESPEN. 2008;3(4):e167-70. [Crossref]
- Papathakis P, Piwoz E. Nutrition and Tuberculosis: A Review of the Literature and Considerations for TB Control Programs; 2008. p.40.
- Gupta V. Clinicoepidemiological study of vesiculobullous disorders in the pediatric age group. Indian Journal of Paediatric Dermatology. 2009;26(1):9-16. [Crossref]
- Phan MN, Guy ES, Nickson RN, Kao CC. Predictors and patterns of weight gain during treatment for tuberculosis in the United States of America. Int J Infect Dis. 2016;53:1-5. [Crossref] [PubMed]

- Cegielski JP, McMurray DN. The relationship between malnutrition and tuberculosis: evidence from studies in humans and experimental animals. Int J Tuberc Lung Dis. 2004;8(3):286-98. [PubMed]
- Snowden FM. Emerging and reemerging diseases: a historical perspective. Immunol Rev. 2008;225(1):9-26. [Crossref] [PubMed]
- Benatar SR, Upshur R. Tuberculosis and poverty: what could (and should) be done? Int J Tuberc Lung Dis. 2010;14(10):1215-21. [PubMed]
- Tanimura T, Jaramillo E, Weil D, Raviglione M, Lönnroth K. Financial burden for tuberculosis patients in low-and middle-income countries: a systematic review. Eur Respir J. 2014;43(6): 1763-75. [Crossref] [PubMed] [PMC]
- Barter DM, Agboola SO, Murray MB, Bärnighausen T. Tuberculosis and poverty: the contribution of patient costs in sub-Saharan Africa--a systematic review. BMC Public Health. 2012;12(1):980. [Crossref] [PubMed] [PMC]
- Samuel B, Volkmann T, Cornelius S, Mukhopadhay S, MejoJose, Mitra K, et al. Relationship between Nutritional Support and Tuberculosis Treatment Outcomes in West Bengal, India. J Tuberc Res. 2016;4(4):213-9. [Crossref] [PubMed] [PMC]
- Ukwaja KN, Modebe O, Igwenyi C, Alobu I. The economic burden of tuberculosis care for patients and households in Africa: a systematic review. Int J Tuberc Lung Dis. 2012;16(6):733-9. [Crossref] [PubMed]
- Elamin El, Ibrahim MI, Sulaiman SA, Muttalif AR. Cost of illness of tuberculosis in Penang, Malaysia. Pharm World Sci. 2008;30(3):281-6. [Crossref] [PubMed]
- Macallan D. Infection and malnutrition. Medicine. 2009;37(10):525-8. [Crossref]
- Macallan DC, McNurlan MA, Kurpad AV, de Souza G, Shetty PS, Calder AG, et al. Whole body protein metabolism in human pulmonary tuberculosis and undernutrition: evidence for anabolic block in tuberculosis. Clin Sci (Lond). 1998;94(3):321-31. [Crossref] [PubMed]
- Ismail IS, Bebakar W, Kamaruddin NJP-MoHM. Clinical practice guidelines on management of obesity. Academy of Medicine of Malaysia, Malaysian Association for the Study of Obesity, Malaysian Endocrine, Society M; 2004. p.57.
- Mohamed-Hussein A, Salama S, Khalil M, Eid S. Malnutrition in tuberculosis: value of fat-free mass and creatinine-height index. Pulmonary Infections. 2016;10(1):58-63. [Crossref]

- Paton NI, Chua YK, Earnest A, Chee CB. Randomized controlled trial of nutritional supplementation in patients with newly diagnosed tuberculosis and wasting. Am J Clin Nutr. 2004;80(2):460-5. [Crossref] [PubMed]
- Kassu A, Yabutani T, Mahmud ZH, Mohammad A, Nguyen N, Huong BT, et al. Alterations in serum levels of trace elements in tuberculosis and HIV infections. Eur J Clin Nutr. 2005;60(5):580-6. [Crossref] [PubMed]
- Visvanathan R, Penhall R, Chapman I. Nutritional screening of older people in a subacute care facility in Australia and its relation to discharge outcomes. Age Ageing. 2004;33(3): 260-5. [Crossref] [PubMed]
- Ismail MN, Chee SS, Nawawi H, Yusoff K, Lim TO, James WP. Obesity in Malaysia. Obes Rev. 2002;3(3):203-8. [Crossref] [PubMed]
- Dargie B, Tesfaye G, Worku AJBN. Prevalence and associated factors of undernutrition among adult tuberculosis patients in some selected public health facilities of Addis Ababa, Ethiopia: a cross-sectional study. BMC Nutr. 2016;2(1):7. [Crossref]
- Gurung LM, Bhatt LD, Karmacharya I, Yadav DK. Dietary practice and nutritional status of tuberculosis patients in Pokhara: a cross sectional study. Front Nutr. 2018;5:63. [Crossref] [PubMed] [PMC]
- World Health Organization (WHO). Guideline: nutritional care and support for patients with tuberculosis. Geneva: WHO Press; 2013. p.55.
- Atif M, Sulaiman SAS, Shafie AA, Ali I, Asif M, Babar Z. Treatment outcome of new smear positive pulmonary tuberculosis patients in Penang, Malaysia. BMC Infect Dis. 2014;14(1):399. [Crossref] [PubMed] [PMC]
- William T, Parameswaran U, Lee WK, Yeo TW, Anstey NM, Ralph AP. Pulmonary tuberculosis in outpatients in Sabah, Malaysia: advanced disease but low incidence of HIV co-infection. BMC Infect Dis. 2015;15:32. [Crossref] [PubMed] [PMC]
- Kennedy N, Ramsay A, Uiso L, Gutmann J, Ngowi FI, Gillespie SH. Nutritional status and weight gain in patients with pulmonary tuberculosis in Tanzania. Trans R Soc Trop Med Hyg. 1996;90(2):162-6. [Crossref] [PubMed]
- Bourke CD, Berkley JA, Prendergast AJ. Immune dysfunction as a cause and consequence of malnutrition. Trends Immunol. 2016;37(6):386-98. [Crossref] [PubMed] [PMC]
- 35. Bass JB Jr, Farer LS, Hopewell PC, O'Brien R, Jacobs RF, Ruben F, et al. Treatment of

tuberculosis and tuberculosis infection in adults and children. American Thoracic Society and the Centers for Disease Control and Prevention. Am J Respir Crit Care Med. 1994;149(5):1359-74. [Crossref] [PubMed]

- Schaberg T, Rebhan K, Lode H. Risk factors for side-effects of isoniazid, rifampin and pyrazinamide in patients hospitalized for pulmonary tuberculosis. Eur Respir J. 1996;9(10):2026-30. [Crossref] [PubMed]
- Asscher AW, Parr GD, Whitmarsh VB. Towards the safer use of medicines. BMJ. 1995;311(7011):1003-6. [Crossref] [PubMed] [PMC]
- Forget EJ, Menzies D. Adverse reactions to first-line antituberculosis drugs. Expert Opin Drug Saf. 2006;5(2):231-49. [Crossref] [PubMed]
- Yee D, Valiquette C, Pelletier M, Parisien I, Rocher I, Menzies D. Incidence of serious side effects from first-line antituberculosis drugs among patients treated for active tuberculosis. Am J Respir Crit Care Med. 2003;167(11): 1472-7. [Crossref] [PubMed]
- Walter-Sack I, Klotz U. Influence of diet and nutritional status on drug metabolism. Clin Pharmacokinet. 1996;31(1):47-64. [Crossref] [PubMed]
- Ramappa V, Aithal GP. Hepatotoxicity related to anti-tuberculosis drugs: mechanisms and management. J Clin Exp Hepatol. 2013;3(1): 37-49. [Crossref] [PubMed] [PMC]
- Mohd Avwar SA, Salmiah MS, Saliluddin SM, Lim PY. Factors delaying sputum conversion in smear positive pulmonary tuberculosis: a systematic review. International Journal of Public Health and Clinical Sciences. 2018;5(3):56-61.
- Kliiman K. Highly Drug-Resistant Tuberculosis in Estonia: Risk Factors and Predictors of Poor Treatment Outcome. Estonia: Council of the Faculty of Medicine, University of Tartu; 2010. p.146.
- Khan A, Sterling TR, Reves R, Vernon A, Horsburgh CR. Lack of weight gain and relapse risk in a large tuberculosis treatment trial. Am J Respir Crit Care Med. 2006;174(3):344-8. [Crossref] [PubMed]
- 45. Van Lettow M, Kumwenda JJ, Harries AD, Whalen CC, Taha TE, Kumwenda N, et al. Malnutrition and the severity of lung disease in adults with pulmonary tuberculosis in Malawi. Int J Tuberc Lung Dis. 2004;8(2):211-7. [PubMed]
- Waitt CJ, Squire SB. A systematic review of risk factors for death in adults during and after tuberculosis treatment. Int J Tuberc Lung Dis. 2011;15(7):871-85. [Crossref] [PubMed]

- Kant S, Gupta H, Ahluwalia S. Significance of nutrition in pulmonary tuberculosis. Crit Rev Food Sci Nutr. 2015;55(7):955-63. [Crossref] [PubMed]
- Tulsky JP, Hahn JA, Long HL, Chambers DB, Robertson MJ, Chesney MA, et al. Can the poor adhere? Incentives for adherence to TB prevention in homeless adults. Int J Tuberc Lung Dis. 2004;8(1):83-91. [PubMed]
- Davidson H, Schluger NW, Feldman PH, Valentine DP, Telzak EE, Laufer FN. The effects of increasing incentives on adherence to tuberculosis directly observed therapy. Int J Tuberc Lung Dis. 2000;4(9):860-5. [PubMed]
- Cantalice Filho JP. [Food baskets given to tuberculosis patients at a primary health care clinic in the city of Duque de Caxias,

Brazil: effect on treatment outcomes]. J Bras Pneumol. 2009;35(10):992-7. [Crossref] [PubMed]

 O'Boyle SJ, Power JJ, Ibrahim MY, Watson JP. Factors affecting patient compliance with anti-tuberculosis chemotherapy using the directly observed treatment, short-course strategy (DOTS). Int J Tuberc Lung Dis. 2002;6(4):307-12. [PubMed]